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Case Report

Are SADI-S and BPD/DS bariatric procedures identical twins or distant relatives? – A case report

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ABSTRACT

Given the common anatomical features and similar short-term weight loss outcomes, Biliopancreatic Diversion with Duodenal Switch (BPD/DS) and Single-Anastomosis Duodenoileal bypass with Sleeve gastrectomy (SADI-S) are considered identical bariatric procedures, apart from technical complexity being lower for SADI-S. In the absence of prospective randomized trials or long-term comparative studies the rationale for choosing between procedures is hampered. Post-bariatric hormonal profiles could contribute to understand the underlying mechanisms and potentially be used as a decision aid when choosing between procedures.

The main aim of this study was to compare the outcomes of BPD/DS and SADI-S, in genetically identical individuals exposed to similar environmental factors.

Two identical twin (T) female patients, one submitted to BPD/DS (T_BPD/DS) and another to SADIS-S (T_SADI-S) were followed up to one year after surgery. Before surgery and at 3, 6 and 12 months after surgery, both patients underwent mixed meal tolerance tests (MMTT) to evaluate postprandial glucose, glucagon and GLP-1 response. In addition, 3 months after surgery, glucose dynamics were assessed using a Flash Glucose Monitoring (FGM) system for 14 days.

The percentage of total weight loss (%TWL) was higher for T_BPD/DS compared to T_SADI-S (34.03 vs 29.03 %). During MMTT, T_BPD/DS presented lower glucose, glucagon, insulin and C-peptide excursions at all timepoints when compared to SADI-S; along with a greater percentage of time within the low glucose range (55.97 vs 39.93 %) and numerically lower glucose variability indexes on FGM (MAG change:0.51 vs 0.63 mmol/l×h^{-1}).

In patients with the same genetic background, BPD/DS was shown to result in greater weight loss than SADI-S. The differences in glucose and enteropancreatic hormone profiles observed after BPD/DS and SADI-S suggest that different mechanisms underlie weight loss.

1. Introduction

Biliopancreatic Diversion with Duodenal Switch (BPD/DS) is the most effective weight loss intervention, but also the most complex bariatric procedure [1]. Single-Anastomosis Duodenoileal bypass with Sleeve gastrectomy (SADI-S) [2] is a simplified version of BPD/DS with lower operative time, morbidity and mortality [3].

Despite the inconsistent advantage of BPD/DS in long-term weight loss and type 2 diabetes (T2D) remission, in the absence of prospective randomized trials or long-term comparative studies, there is currently no high-level evidence to support the choice between the two techniques nor a solid demonstration of SADI-S long-term effectiveness [4–6], as recognized by the IFSO 2020 Position Statement [7,8].

Until further evidence is available, disclosing the mechanisms

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underlying weight loss and obesity-related co-morbidity remission associated with different procedures through the analysis of hormone profiles, could contribute for the decision on which procedure could be the most appropriate for each patient [9,10].

Body mass index is known to be a highly heritable trait. Furthermore, obesogenic environments at both childhood and adulthood increase the risk of obesity in genetically susceptible individuals [11,12]. Twin studies provide a strong basis for exploring treatment responses, while controlling for the genetic variability. Moreover, twins raised in the same family household have the advantage of providing an additional control for early life environmental cues. Therefore, clinical trials enrolling co-twin controls to assess an intervention effect have a statistical power seven times greater than randomized controlled trials in unrelated individuals [13,14].

The primary aim of this study was to compare the outcomes of BPD/DS and SADI-S, in genetically identical individuals raised and living in the same household. As secondary aim, postprandial hormones and glycemic variability were evaluated, to gather unbiased data on mechanistic differences between procedures.

This case report has been reported in line with the SCARE Criteria [15].

2. Methods

Two female monozygotic twin patients that shared the same household and workplace, were randomly allocated to be submitted to BPD/DS or SADI-S, as part of the ongoing interventional clinical trial SURIDIAB2-Surgical Innovation for Diabetes Treatment 2 (ClinicalTrials.gov Identifier: NCT04712409), which aims to compare enteroendocrine dynamics after BPD/DS and SADI-S. For both surgeries, the sleeve gastrectomy was done over a 36 French Boogie, starting 4 cm proximal to the pylorus. The SADI-S was performed with a 300 cm common channel while the BPD-DS was performed with a common limb of 100 cm and an alimentary limb of 200 cm. For both procedures, ligation of the right gastric vessels is routinely performed.

This study was approved by the institutional review board (CA-110/2020–0t_MP/AC) and informed consent was obtained from the participants included. Patients underwent surgery on the same day and by the same surgeons, as previously described [6].

2.1. Glucose and hormone response to a liquid mixed meal

A liquid mixed meal tolerance test (MMTT) (Fresubin Energy Drink, 200 mL, 300 kcal; Fresenius Kabi) was performed before and 3, 6 and 12 months after surgery. Whole blood glucose was measured using a glucometer (Freestyle Precision Neo Glucose meter, Abbott, USA). Insulin and C-peptide were quantified by an electrochemiluminescence. Glucagon and total glucagon-like peptide-1 (GLP-1) levels were measured by radioimmunoassay (RIA) targeting the C-terminal of glucagon (antiserum 4305 [16]) and the C-terminal of GLP-1 (antiserum 89390 [17]), respectively.

2.2. Glycemic variability analysis

Flash glucose monitoring (FGM, FreeStyle Libre, Abbott Diabetes Care) over 14 days was conducted 3 months after surgery. Mathematical computation of the FGM data, namely mean absolute glucose change (MAG change), continuous overlapping net glycemic action (CONGA1) and mean of daily differences (MODD) were calculated to evaluate short-term, intra-daily and inter-daily glucose variability patterns [18]. Low blood glucose index [adjusted] [$LBGI_{FGM}GT$], [adjusted], high blood glucose index [adjusted] [$HBGI_{FGM}GT$] and average daily risk ratio [adjusted] [$ADRR_{FGM}GT$] were obtained to evaluate glucose deviations from target range towards hypoglycemia, hyperglycemia or in both directions, respectively.

3. Results

3.1. Anthropometric and biochemical data

Despite similar pre-operative BMI, the T_BPD/DS presented higher %EBMIL (70.84 vs 58.02 %) and %TWL (34.03 vs 29.03 %) when compared to T_SADI-S 12 months after surgery (Table 1). In both patients HOMA-IR decreased towards normal values 12 months after surgery.

3.2. Glycemic variability

During FGM, there were no values on the hyperglycemia range. T_BPD/DS presented a greater percentage of time with glucose values under 70 mg/dL (55.97 vs 39.93 %) when compared to T_SADI-S (Table 2). Glucose deviations from target towards the low glucose range, represented by the $LBGI_{FGM}GT$, were 1.6 times higher in T_ BPD/DS when compared to T_SADI-S. Short-term (MAG change), inter-hourly (CONGA1) and inter-daily (MODD) glucose variability patterns were numerically higher in T_SADI-S (Table 2).

3.3. Glucose and hormone response to the mixed meal

Before surgery, fasting and postprandial glucose and hormone dynamics were similar in both patients (Fig. 1 and Supplementary table 1). After surgery, T_BPD/DS presented lower glucose, insulin and C-peptide excursions during the MMTT, at all follow-up timepoints. T_BPD/DS also presented lower GLP-1 and glucagon excursions at all post-operative timepoints, with a sole exception at 3 months of follow-up, which was accompanied by dumping syndrome symptoms, namely nausea, abdominal pain and diarrhea, during the 30–45 min' interval, after meal (Fig. 1 and Supplementary table 1).

4. Discussion

Precision medicine and tailored surgery are on the edge of transforming clinical practice. In the quest to foresee which is the most effective and safe bariatric intervention for each individual patient, genetically identical individuals sharing the same environmental exposures represent perfect models for comparing surgical interventions. Therefore, the twin siblings living in the same household, submitted to BPS-DS or SADI-S, allowed direct comparison of weight loss and safety outcomes of different bariatric procedures.

In this context, BPD/DS is reported to result in greater weight loss for up to two years after surgery [6] and the same tendency seems is observed here. Despite the weight loss differences both patients were satisfied with bariatric surgery outcomes.

The entero-pancreatic hormone secretion profiles elicited by the two surgeries suggest that these are likely to achieve weight loss via different mechanisms of action, with less pronounced glucose and gut hormone postprandial excursions and lesser glycemic variability after BPS-DS. Nevertheless, the two twins experienced complete reversal of insulin resistance. Indeed, up to 2 years after surgery no significant differences in T2D remission were reported between BPS-DS and SADI-S in a retrospective series, although weight loss and T2D remission rate being greater in patients with greater BMIs ($BMI>55\ kg/m^2$) [4]. Of notice, weight loss and antidiabetic effectiveness of SADI-S was demonstrated to be marginally lower when compared to BPS-DS from the 3–5 years after surgery [19].

Furthermore, post-absorptive enteropancreatic hormone and metabolite profile also diverged between procedures. After BPD/DS glucose, GLP-1, glucagon, insulin and C-peptide postprandial excursions was lower when compared to SADI-S. These differences observed could be attributed to a longer absorptive common limb in SADI-S with greater meal and bile acids exposure triggering GLP-1 release. Since both glucose and GLP-1 stimulate insulin secretion, these provide a possible

Table 1
Anthropometric and biochemical features of the subjects.

	T_BPD-DS	T_SADI-S
Age at surgery (years)	30	30
Gender	Female	Female
Weight (kg)		
Pre-operative	144	155
3 months	121 (−23)	134 (−21)
6 months	107 (−37)	116 (−39)
12 months	95 (−49)	110 (−45)
BMI (kg/m^2)		
Pre-operative	48.11	50.04
3 months	40.43 (−7.68)	43.26 (−6.78)
6 months	35.75 (−12.36)	37.54 (−12.50)
12 months	31.74 (−16.37)	35.51 (−14.53)
TWL (%)		
3 months	15.97	13.55
6 months	25.69	25.16
12 months	34.03	29.03
EBMIL (%)		
3 months	33.25	27.08
6 months	53.49	50.28
12 months	70.84	58.02
Hg (g/dL)		
Pre-operative	13.2	12.5
3 months	12.2 (−1.0)	12.2 (−0.3)
6 months	12.0 (−1.2)	12.8 (+0.3)
12 months	12.9 (−0.3)	13.1 (+0.6)
Fasting glucose (mg/dL)		
Pre-operative	83	94
3 months	79 (−4)	93 (−1)
6 months	74 (−9)	83 (−11)
12 months	90 (+7)	92 (−2)
A1c (%)		
Pre-operative	5.3	5.3
3 months	4.8 (−0.5)	4.9 (−0.4)
6 months	4.6 (−0.7)	4.8 (−0.5)
12 months	4.7 (−0.6)	5.0 (−0.3)
Fasting insulin (μUI/mL)		
Pre-operative	12.5	11.4
3 months	4.1 (−8.4)	7.7 (−3.7)
6 months	7.3 (−5.2)	8.4 (−3.0)
12 months	3.0 (−9.5)	5.1 (−6.3)
HOMA1-IR		
Pre-operative	2.56	2.62
3 months	0.80 (−1.76)	1.76 (−0.86)
6 months	1.32 (−1.24)	1.72 (−0.90)
12 months	0.66 (−1.90)	1.16 (−1.46)
HOMA1-β (%)		
Pre-operative	224.46	134.03
3 months	92.03 (−132.43)	92.04 (−41.99)
6 months	237.27 (+12.81)	150.75 (+16.72)
12 months	39.33 (−185.13)	63.19 (−70.84)
B12 vitamin (pg/mL)		
[normal range: 189.0–883.0]		
3 months	393	240
6 months	432	223
12 months	648	178
25-OH-D vitamin (ng/mL)		
[normal range: 10.0–65.0]		
3 months	46.20	56.30
6 months	51.80	39.70
12 months	49.40	31.50
Vitamin A (mg/L)		
[normal range: 0.3–1.0]		
3 months	0.33	0.55
6 months	0.17	0.21
12 months	0.33	0.41
Total proteins (g/dL)		
[normal range: 6.4–8.3]		
Pre-operative	7.5	7.1
3 months	6.3 (−1.2)	6.9 (−0.2)
6 months	6.0 (−1.5)	6.5 (−0.6)
12 months	6.7 (−0.8)	7.2 (+0.1)
Albumin (g/dL)		
[normal range: 3.5–5.0]		
Pre-operative	4.4	4.2
3 months	3.5 (−0.9)	3.8 (−0.4)
6 months	3.2 (−1.2)	3.8 (−0.4)
12 months	3.9 (−0.5)	4.2 (0.0)
Folic acid (ng/mL)		
[normal range: 3.0–20.0]		
3 months	3.5	4.6
6 months	3.5	3.2
12 months	10.4	2.7

BMI: Body mass index; TWL: Total weight loss; EWL: Excess of weight loss; HOMA-IR: Homeostasis Model Assessment for Insulin Resistance (Reference value: <1.85 for female; HOMA-β: Homeostasis Model Assessment for β-cell function (Reference values: >86.2 % for female). In parentheses are the differences between that value in comparison to the baseline value.

Table 2
Flash glucose monitoring data in twin patients.

	T_BPD-DS	T_SADI-S
Glucose < 54 mg/dL (time %)	2.19	0.00
Glucose 54–69 mg/dL (time %)	53.78	39.93
Glucose 70–140 mg/dL (time %)	46.22	60.07
Glucose > 140 mg/dL (time %)	0.00	0.00
MAG change (mmol/L × h^{-1}) (Reference value: 0.5 – 2.2)	0.51	0.63
CONGA1	0.44	0.56
MODD	0.38	0.41
$LBGI_{FGM}GT$	12.08	7.69
$HBGI_{FGM}GT$	0.00	0.02
$ADRR_{FGM}GT$	28.34	19.49

MAG change: mean absolute glucose change; CONGA1- continuous overlapping net glycemic action; MODD - mean of daily differences; $ADRR_{FGM}GT$ - adjusted average daily risk ratio; $LBGI_{FGM}GT$ - adjusted low blood glucose index; $HBGI_{FGM}GT$ – adjusted high blood glucose index.

explanation for the higher insulin levels observed in the patient submitted to SADI-S. Moreover, these post-absorptive profiles are in agreement with those previously reported by us after these two bariatric surgery procedures in genetically unrelated individuals [9].

Lower interstitial glucose levels and glucose variability indices were also observed in the twin submitted to BPD/DS. Moreover, the patient submitted to BPD/DS spent 55.97 % of the time with interstitial glucose levels below 70 mg/dL but did not report symptoms compatible with reactive hyperinsulinemic hypoglycemia, in agreement with the lower postprandial glucose and insulin levels.

Furthermore, the twin submitted to BPD/DS experienced symptoms fulfilling the dumping criteria during the MMTT conducted at 3 months after surgery. Interestingly, dumping syndrome symptoms accompanied the GLP-1 and insulin peak levels during MMTT. Indeed, GLP-1 was previously proposed to be involved in early dumping syndrome [20]. This profile was only observed during the first MMTT performed after BPD/DS, suggesting that a metabolic adaptation occurred, at the 3–6 months' interval after surgery, which led to decreased postprandial GLP-1 secretion and consequently of insulin secretion. Although the T-SADI-S presented higher GLP-1 levels during the MMTT, no symptoms suggesting early dumping syndrome were reported. Thus, after SADI-S, such a metabolic adaptation could have occurred at an earlier time point after surgery, given that the intestinal rearrangement is less disruptive of the normal gastrointestinal anatomy and biliary physiology as compared to BPD/DS.

Considering our primary aim of comparing the effectiveness and safety of two different surgical procedures in genetically identical individuals, we were able to demonstrate that BPD/DS resulted in greater weight loss, yet in similar improvement of insulin resistance as compared to SADI-S. Furthermore, the greatest differences between the twins were observed at post-absorptive entero-pancreatic hormone profile and in parallel different metabolic outcomes could be predicted.

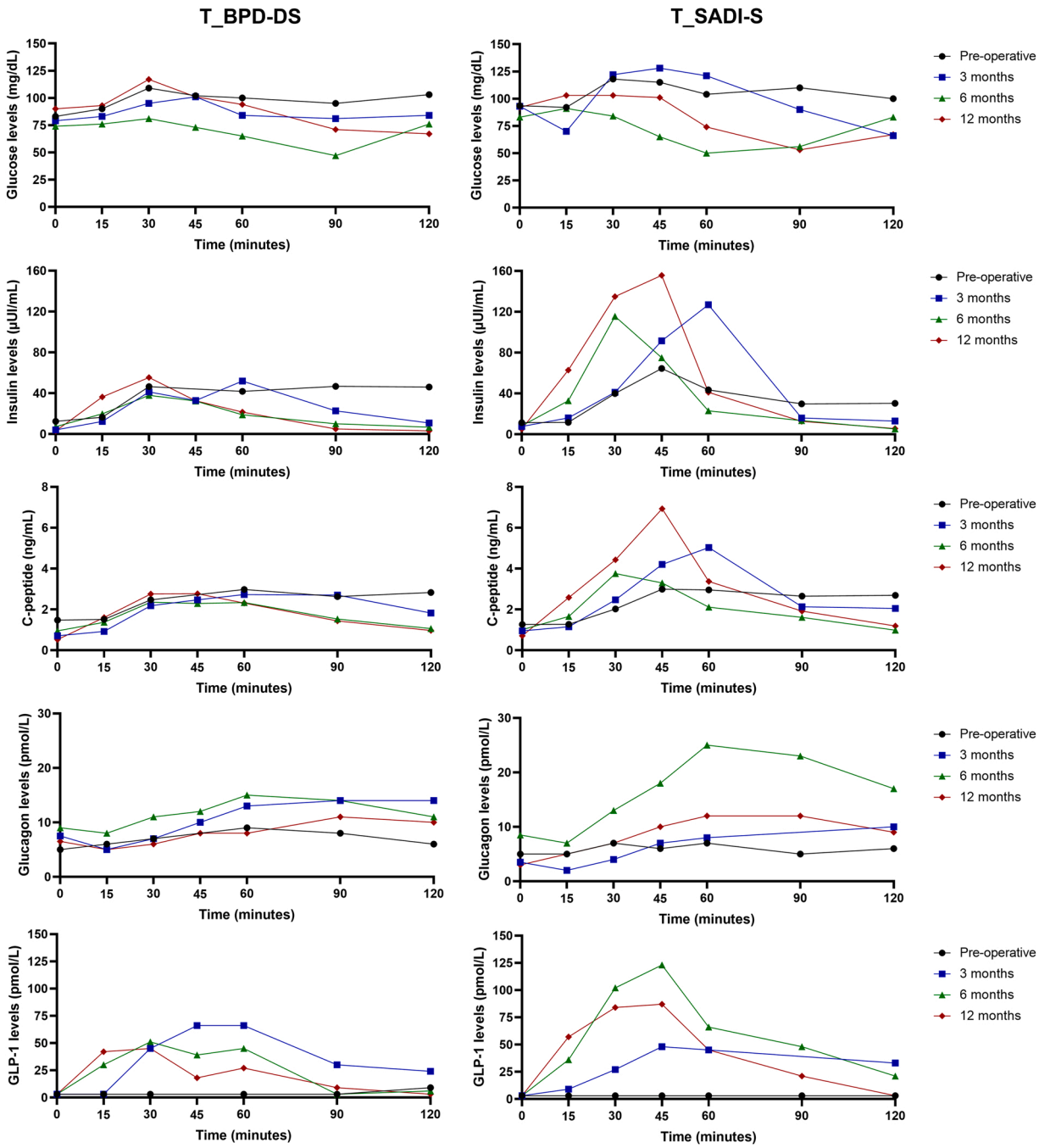

Fig. 1. Peripheral levels of glucose, insulin, C-peptide, glucagon and glucagon like peptide-1 (GLP-1) in the twin subjects, before and after a standard mixed-meal served at t = 0 min.

These could also provide a possible explanation for the weight loss differences observed. It remains to be demonstrated whether the hormonal profiles that differentiate BPD/DS and SADI-S will have an impact at long-term weight loss or obesity co-morbidities resolution.

5. Conclusion

In monozygotic twin patients, with the same genetic and similar environmental background, BPD/DS was shown to be more effective at achieving greater weight loss with lower glycemic variability as compared to SADI-S. The different entero-pancreatic hormone secretion profiles elicited by BPD/DS and SADI-S suggest that these procedures involve different weight loss mechanisms that could result in distinctive outcomes, despite previous reports depicting no differences in short term anthropometric outcomes in genetically unrelated individuals.

Ethical Statement

The authors declare that all experiments on human subjects were conducted in accordance with the Declaration of Helsinki, http://www.wma.net, and that all procedures were carried out with the adequate understanding and written consent of the subjects.

The authors also certify that formal approval to conduct the experiments described has been obtained from the human subjects review board of their institution (CA-110/2020–0t_MP/AC) and could be provided upon request.

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CRediT authorship contribution statement

Marta Guimarães: Conceptualization, Data curation, Methodology, Investigation, Writing – original draft. **Ana M. Pereira:** Data curation, Methodology, Investigation. **Sofia S. Pereira:** Formal analysis, Investigation, Writing – review & editing. **Rui Almeida:** Data curation, Methodology, Investigation. **Carolina B. Lobato:** Investigation, Methodology, Writing – review & editing. **Bolette Hartmann:** Investigation, Methodology, Writing – review & editing. **Jens J. Holst:** Investigation, Methodology, Resources, Writing – review & editing. **Mário Nora:** Investigation, Methodology, Resources. **Mariana P. Monteiro:** Conceptualization, Resources, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.orcp.2023.02.004.

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